

## PARENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>01-0834EP 05</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/PT 01/00008</b>	International filing date ( <i>day/month/year</i> ) <b>17/05/2001</b>	(Earliest) Priority Date ( <i>day/month/year</i> ) <b>17/05/2000</b>
Applicant <b>INSTITUTO SUPERIOR TECNICO et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  **Certain claims were found unsearchable** (See Box I).

3.  **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

PROCESS FOR THE CONTINUOUS PRODUCTION OF DIPEPTIDE CRYSTALS IN A MEMBRANE AND HYDRO-CYCLONE RACTOR USING A PEPTIDASE

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

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None of the figures.

**INTERNATIONAL SEARCH REPORT**

International application No.

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**Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)**

The invention relates to a process for the production of dipeptide crystals (generic formula AcXYNH<sub>2</sub>) with high purity (>95%), by enzymatic synthesis with a protease in organic media of reversed micelles, starting from derivatives of the two constituent amino acids (AcXOEt and YNH<sub>2</sub>). A membrane and hydro-cyclone reactor was designed which enables the continuous and simultaneous synthesis and crystallisation of the dipeptides. The dipeptide crystals thus prepared are continuously removed and further separated from the remaining liquid by filtration or centrifugation. After drying, the crystals are dissolved in hot methanol. By decreasing the temperature, the dipeptide re-crystallises, originating a high purity product. After re-crystallisation the product is filtered and dried.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/01/00008

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12P21/02 C07K1/36 C07K1/02 C12M1/12 B04C3/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12P C07K C12M B04C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ✓	SERRALHEIRO M L M ET AL: "Continuous production and simultaneous precipitation of a dipeptide in a reversed micellar membrane reactor." ENZYME AND MICROBIAL TECHNOLOGY, vol. 24, no. 8-9, June 1999 (1999-06), pages 507-513, XP001010232 ISSN: 0141-0229 cited in the application the whole document ---	1, 2, 4, 5, 7
Y ✓	FR 2 679 235 A (AJINOMOTO KK) 22 January 1993 (1993-01-22) the whole document ---	3, 6
Y ✓	FR 2 679 235 A (AJINOMOTO KK) 22 January 1993 (1993-01-22) the whole document ---	3, 6

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

### ° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

6 July 2001

Date of mailing of the international search report

17/07/2001

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

Smalt, R

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/01/00008

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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X ✓	FELICIANO A S ET AL: "The effect of stirring and seeding on the AcPheLeuNH <sub>2</sub> synthesis and crystallization in a reversed micellar system." ENZYME AND MICROBIAL TECHNOLOGY, vol. 27, no. 3-5, August 2000 (2000-08), pages 264-269, XP001010217 ISSN: 0141-0229 cited in the application the whole document ----	1,2,4,5, 7
A ✓	DE 40 14 564 C (FORSCHUNGSZENTRUM JÜLICH /GMBH, JÜLICH, DE) 18 July 1991 (1991-07-18) the whole document ----	
A ✓	FELICIANO A S ET AL: "Quantitative structure activity relationships in the synthesis of AcXYNH-2 dipeptides by alpha-chymotrypsin in reversed micelles." ENZYME AND MICROBIAL TECHNOLOGY, vol. 21, no. 4, 1997, pages 284-290, XP001010223 ISSN: 0141-0229 cited in the application the whole document -----	

**INTERNATIONAL SEARCH REPORT**

Inform patent family members

International Application No

PCT [REDACTED] 01/00008

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
FR 2679235	A	22-01-1993	JP	2958789 B	06-10-1999
			JP	3216195 A	24-09-1991
			US	5547858 A	20-08-1996
			AU	639809 B	05-08-1993
			AU	8030391 A	28-01-1993
			BR	1100232 A	01-08-2000
			BR	9103114 A	24-02-1993
DE 4014564	C	18-07-1991	CA	2041875 A	08-11-1991
			DE	59107525 D	18-04-1996
			DK	456138 T	22-07-1996
			EP	0456138 A	13-11-1991
			JP	4311390 A	04-11-1992
			US	5369016 A	29-11-1994
			US	5190875 A	02-03-1993

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International Application No PCT/PT 01/00008
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		-/-

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- \*&\* document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 July 2001	17/07/2001
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  Smalt, R

## INTERNAL INTERNAL SEARCH REPORT

International Application No.  
PCT/PT 01/00008

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

(national application No)

PCT/PT 01/00008

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
FR 2679235 A	22-01-1993	JP 2958789 B		06-10-1999
		JP 3216195 A		24-09-1991
		US 5547858 A		20-08-1996
		AU 639809 B		05-08-1993
		AU 8030391 A		28-01-1993
		BR 1100232 A		01-08-2000
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DE 4014564 C	18-07-1991	CA 2041875 A		08-11-1991
		DE 59107525 D		18-04-1996
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		US 5369016 A		29-11-1994
		US 5190875 A		02-03-1993